Journal of Institute of Science and Technology, 28(1), 31-43 (2023)
ISSN: 2467-9062 (print), e-ISSN: 2467-9240
https://doi.org/10.3126/jist.v28i1.49044

Research Article

ESTIMATING THE EFFECTS OF NONPHARMACEUTICAL INTERVENTIONS OF COVID-19 IN SUDURPASHCHIM PROVINCE, NEPAL

Nar Bahadur Chanda[1], Khagendra Adhikari[2,*], Ramesh Gautam[3], Anjana Pokharel[4], Kedar Nath Uprety[5]
[1]Khaptad Multiple Campus, Tribhuvan University, Nepal
[2]Amrit Science Campus, Tribhuvan University, Kathmandu, Nepal
[3]Ratna Rajya Laxmi Campus, Tribhuvan University, Kathmandu, Nepal
[4]Padma Kanya Multiple Campus, Tribhuvan University, Kathmandu, Nepal
[5]Central Department of Mathematics, Tribhuvan University, Kathmandu, Nepal
Correspondence: khadhikari51@gmail.com
*(**Received**: February 23, 2022; **Final Revision**: March 26, 2023; **Accepted**: June 16, 2023)*

ABSTRACT

Due to ongoing viral evolution and frequent outbreaks, responding to the pandemic has been challenging for countries with limited resources, like Nepal. In this study, we retrospectively estimated the impact of nonpharmaceutical interventions (NPIs) in Sudurpashchim province of Nepal using COVID-19 second wave data (20 March-31 August 2021) by using the mathematical model. We estimated extremely low (2%) detection of new cases in Sudurpashchim, and only 10% border screening with Antigen tests among the returnees in Sudurpashchim from India during the Delta surge which was not sufficient to lower the burden of the pandemic. The lockdown implemented during the pandemic was successful in lowering the disease burden. The control interventions were effective which reduced the 34% of new cases and 28% of active cases during the peak time and overall cases by 12.3% from 20 March-31 August 2021. During the peak of the pandemic, control intervention reduced the number of patients in regular beds by 27%, ICU by ~ 31%, and ventilators admissions each by ~33%. Our results explore that, without sufficient detection of new cases in the community, border screening alone is not sufficient for the diseases control. Therefore, in the absence of pharmaceutical interventions, it is important to combine social distance with adequate case detection, which is made even more effective by perfect border screening, to reduce the burden of the pandemic.

Keywords: COVID-19, Nepal, nonpharmaceutical interventions, Sudurpashchim

INTRODUCTION

The novel corona virus (SARS-CoV-2) that caused the COVID-19 pandemic is still spreading throughout the world in multiple waves. By September 1, 2021, the pandemic had already caused more than 219 million cases and 4.55 million fatalities worldwide (Worldometer, 2021; Adhikari, *et al.*, 2022). Despite significant management and control efforts, the second wave of COVID-19, which is caused by various virus variants that are highly contagious, has primarily affected the world due to the Delta variant (B.1.617.2) (Kang, *et al.*, 2021; Mindermann, *et al.*, 2021; Ewen, 2021; Sara *et al.*, 2021; WHO, 2021). After spreading to more than 30 countries, the World Health Organization (WHO) declared the Delta variant a global concern on May 10, 2021 (Nebehay & Farge, 2021).

Nepal consists of seven provinces, each of which was affected differently by the pandemic during the Delta surge. Sudurpashchim province situated on the far western region of Nepal (Fig. 1) is one of the most underdeveloped provinces of Nepal has two major official entry points (Gaddachauki and Trinagar) in the Indo-Nepal border along with two minor entry points (Julaghat and Darchula). Due to the open border provision with India, there is always in and out flux of seasonal migrant workers. In some communities of this region, 50-80 percent of households have at least one relative who works in India; the majority of these migrants migrate seasonally (Vaidya & Wu, 2011).

The second wave caused by the Delta variety started in Nepal in April 2021. Nepal is a developing country with an open porous border with India, where the Delta was first noticed (Poudel *et al.*, 2004). In the middle of April 2021, as cases in India were steadily on the rise, pilgrims from Nepal made their way to the north of India for the Kumbha Mela, a Hindu festival that draws millions of visitors (Khare, 2021). Their influx through the various entry points across the Indo-Nepal borders, particularly in Sudurpashchim province, along with that of the seasonal migrant workers, resulted in the second surge (Poudel *et al.*, 2004). As new cases started to raise in the neighboring country India from the beginning of March 2021, the Government of Nepal (GoN) started conducting antigen tests for returnee migrants along the Nepal-India border. Fig. 2 displays the daily antigen tests and instances of positive cases discovered at the two primary official entry points of the Sudurpashchim province from 1 April 2021. Figure 3 illustrates the noticeably high antigen test positive rate and the significant community transmission of the novel variant in India.

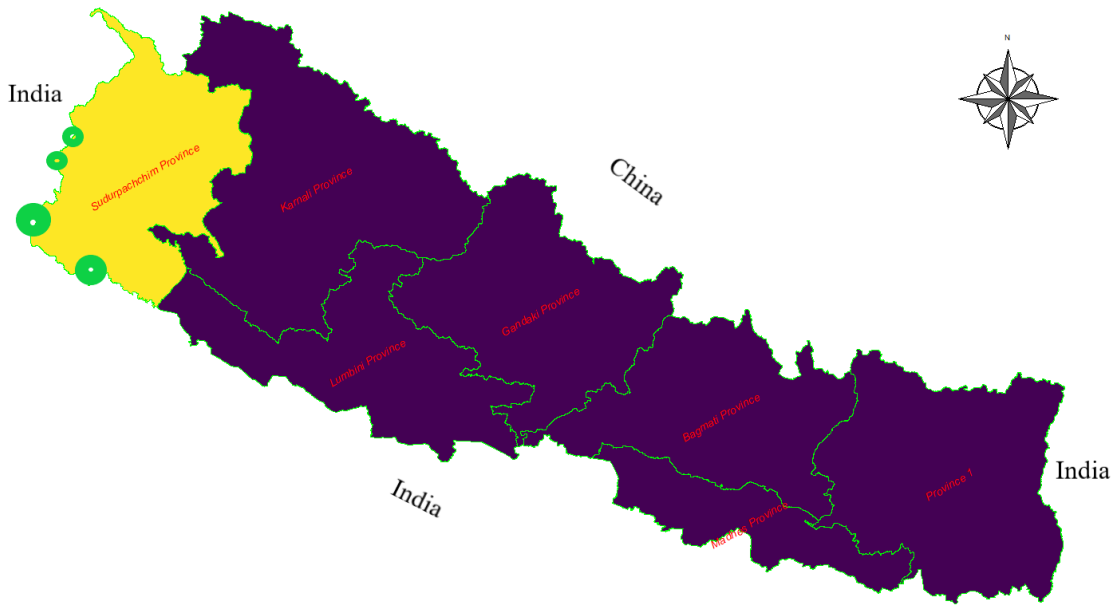

Figure 1. Map of Nepal with highlighted Sudurpashchim province. The data (shapefile format) for the map was obtained from the government of Nepal's official website (urlhttp://http dos.gov.np) (Accessed on April 23, 2021). The map was then created in R 4.3.1 using the cartography package. The Sudurpashchim province is represented by the yellow region. The large circles represent the major official entry points (Trinagar (left) and Gaddachauki (right)), while the small circles represent minor entry points (Julaghat (lower), Darchula (upper) border crossings)

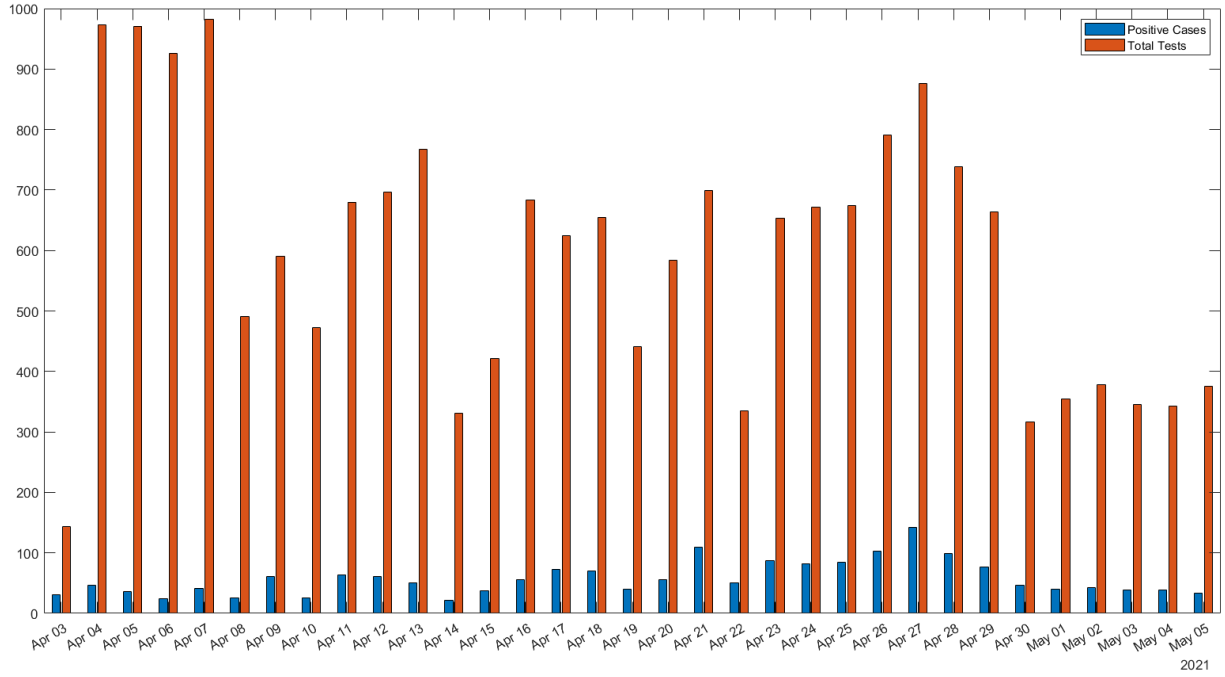

Figure 2. Total no. of daily Antigen tests in border between Nepal and India and COVID-19 positive cases

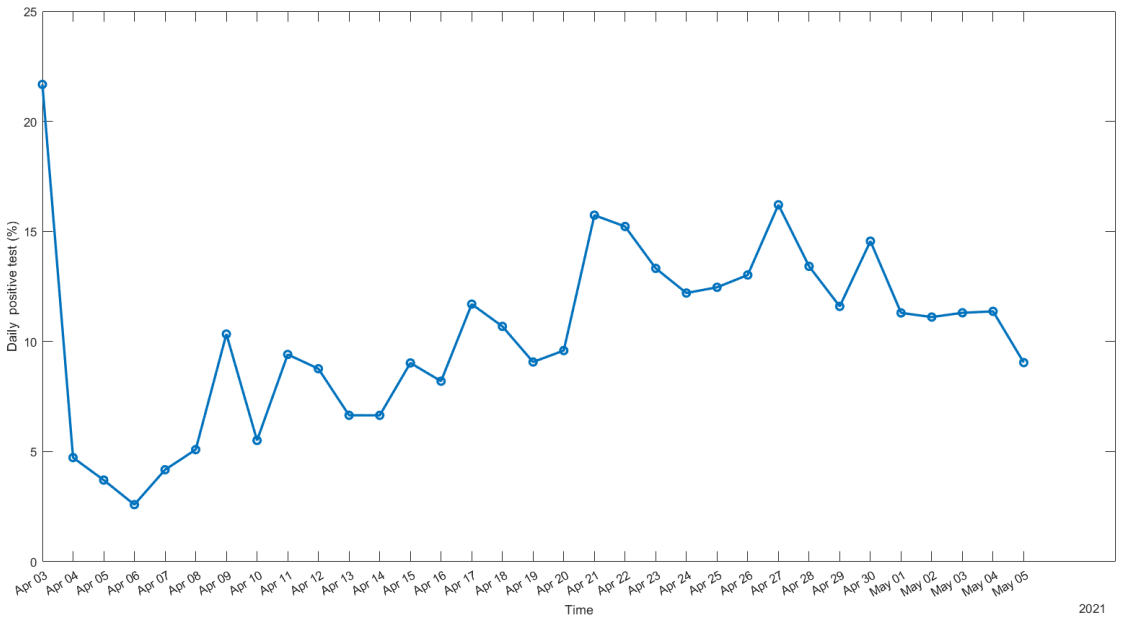

Figure 3. Total percentage of positive cases in the Antigen test at border between Nepal and India

Despite the border screening, COVID-19 cases surged very rapidly in Nepal as well as Sudurpashchim province. To slow the exponential growth of new cases, on April 29, 2021, the GoN imposed the lockdown, beginning in Kathmandu (Aljazeera, 2021). Immediately after, Sudurpashchim's local government imposed the lockdown in some areas, and it was later expanded to other areas (Sudurpashchim Khabar, 2021a). Despite the control interventions, the recorded new cases rose to 1052 on May 17, 2021, with a huge shortage of healthcare facilities, particularly hospital beds and oxygen (Sudurpashchim Khabar, 2021b). This area, therefore, presents us with a unique opportunity for the retrospective study to gain precious insights into the specific pandemic transmission and evaluate the efficacy of control interventions that would be useful in designing policies for the control of spread and proper management of healthcare facilities for future pandemics. In fact, compartment models have long been used to study the dynamics of disease transmission, understand how diseases spread, and aid in the development of curative and preventative measures (Adhikari *et al.*, 2021a; Gautam *et al.*, 2022; Pantha *et al.*, 2021; Pokharel *et al.*, 2022).

In this study, we investigated the dynamics of COVID-19 transmission in Sudurpashchim province using a data-driven modeling approach. We validated our model with Sudurpashchim province data and estimated key model parameters. We estimated the effective reproduction number and used our model to investigate how control interventions helped Sudurpashchim province in coping with the additional burden of the pandemic during the Delta surge.

MATERIALS AND METHODS

Data source

The data used in this study was obtained from the Ministry of Health and Population (MoHP) of the Government of Nepal (MoHP, 2021a). The Government of Nepal started the screening at different border checkpoints from the beginning of the Delta surges including two checkpoints Gaddachauki and Trinagar of Sudurpashchim. The Sudurpashchim province started the lockdown on 29 April 2021 and returned to the almost no-policy state after the long-route buses and national flights were fully open except the resumed of Schools on September 1, 2021 (Sudurpashchim Khabar, 2021a). We considered the data from March 20, until August 31, 2021. The data including antigen tests, new cases, and the cumulative cases were used in our model fitting and simulation. The MoHP data did not include province-level positive cases for Antigen, and the various reports (Sudurpashchim Khabar, 2021b; MoHP, 2021b; Neupane, *et al.*, 2021) indicate that 15% more cases were found via the Antigen test, we added 15% more cases to the published data.

Transmission dynamics model

To develop a transmission dynamics model based on the SEIR framework, the population of this region is divided into six distinct compartments: susceptible (S), exposed (E), recorded infectious (I_R), non-recorded infectious (I_N), recovered (R), and Migrant (M). The immigrant workers from India enter this region at the rate of λ. Among the immigrants (λ), a portion ϕ is tested by the antigen, and the rest (1 -ϕ) entered to the community without the antigen test. The portion ρ of immigrants with a positive

test result entered the recorded infected class (I_R) and the remaining (1-ρ) portion of immigrants with negative test result entered the susceptible class. Among immigrants without antigen test, (1-τ) portion entered the susceptible and τ portion to the non-recorded infectious class I_N. χ_1 and χ_2 represent the death due to COVID-19 in I_R and I_N compartments respectively. The transmission rate from recorded infected individuals and non-recorded infected individuals are denoted by β_1 and β_2 respectively. The exposed individuals become infectious at the rate of δ, among which a portion θ is recorded and the remaining (1-θ) remain in the non-recorded class. The latency period is $\frac{1}{\delta}$ and the infectious period of the infected individuals of the recorded and non- recorded infectious class is $\frac{1}{\eta}$. The schematic diagram of the model is shown in Fig. 4.

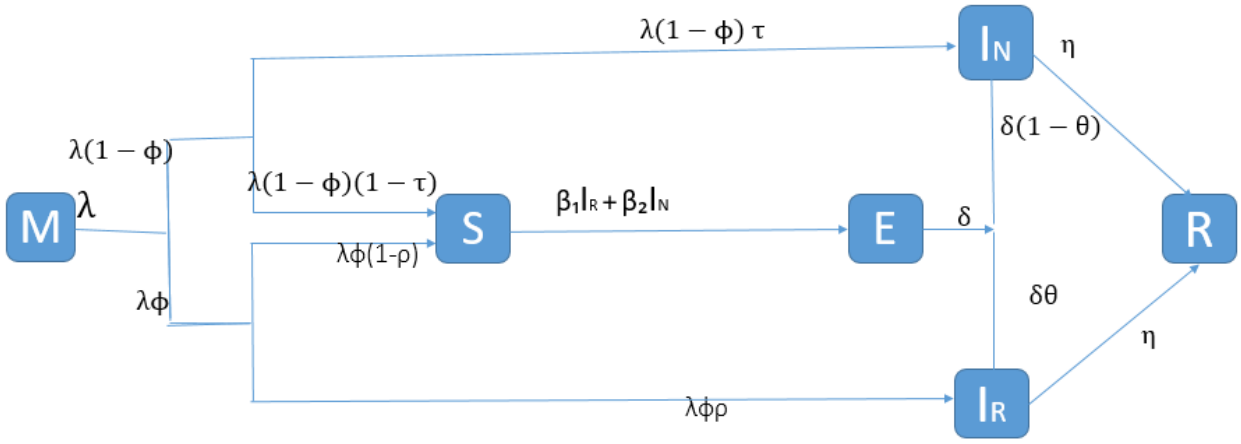

Figure 4. The compartmental diagram of the model. The arrow represents the transfer from one compartment to another

Mathematical Formulation

From the model we obtain the following system of ordinary differential equations

$$\frac{dS}{dt} = \Lambda + \lambda(1-\phi)(1-\tau)M + \lambda\phi(1-\rho)M - \frac{(\beta_1 I_R + \beta_2 I_N)}{S+E+I_R+I_N+R} - \mu S \quad \ldots\ldots\ldots\ldots\ldots(1)$$

$$\frac{dE}{dt} = \frac{(\beta_1 I_R + \beta_2 I_N)}{S+E+I_R+I_N+R} - \delta E - \mu E \quad \ldots\ldots\ldots\ldots\ldots (2)$$

$$\frac{dI_R}{dt} = \delta\theta E + \lambda\phi\rho M - (\eta + \chi_1 + \mu) I \quad \ldots\ldots\ldots\ldots (3)$$

$$\frac{dI_N}{dt} = \delta(1-\theta) E + \lambda(1-\phi)\tau M - (\eta + \chi_2 + \mu) I_N \ldots\ldots\ldots\ldots\ldots (4)$$

$$\frac{dR}{dt} = \eta(I_N + I_R) - \mu R \ldots\ldots\ldots\ldots (5)$$

$$\frac{dM}{dt} = -\lambda M - \mu M \ldots\ldots\ldots\ldots\ldots\ldots (6)$$

Parameter estimation and model fitting to data

Since the new cases began to increase in Sudurpashchim province from the last week of March 2021, we took March 20, 2021, as the initial time (t=0) to initiate the first wave. The total population of Sudurpashchim in the census year 2021 is 2711270 (CBS, 2022). About 3.5 million Nepalese live in India as migrant workers (Kunwar, 2015; Prasain, 2021) and most of the migrant workers are from Sudurpashchim and Karnali Provinces, so we took 50,0000 population in Migrant class. Using 14.4% [95% CI: 11.8-17.0] seroprevalence found in the October 2020 (MoHP, 2021b), our previous model (Adhikari *et al.*, 2022), allowed us to estimate the seroprevalence on March 20, 2021, to be ~ 24%. We deducted both seroprevalence and migrant population from the total population and took the initial susceptible population as 1377800 for this study.

The lockdown from the Kailali and Kanchanpur districts of the province was started on March 29, 2021, and gradually extended to almost all parts of the province. The lock-down option gradually dropped as the number of new cases lowered, allowing people to resume their regular daily activities. We can incorporate these shifts in government policy into our model by assuming the following transmission rates of unrecorded cases (β_2):

$$\beta_2(t) = \begin{cases} \beta_2(0), & \text{for } 0 \le t < t_0 \\ \beta_2(0)\left((1-c_b)e^{\left(-r(t-t^0)\right)} + c_b\right), & \text{for } t_0 \le t < t_1 \\ (\beta_2(t_1) - \beta_2(0))e^{(-r_1(t-t_1))} + \beta_2(0), & \text{for } t \ge t_1 \end{cases}$$

where, t_0 and t_1 represent starting and ending times of the lockdown respectively. We took $c_b = 0.3$ assuming up to 70% reduction on contacts during the prolonged lockdown period, r and r_1 are rates of reduction of transmission rate in time intervals $t_0 \le t < t_1$ and $t \ge t_1$. The transmission rate of recorded infectious was assumed to be reduced by 80% than that of the non-recorded. We calculated the Positivity rate of the Antigen test (ϱ) from the data who were screened at the border. The incubation and recovery period were taken from the literature and the remaining parameters were estimated by using the nonlinear least square method.

For the model fitting the data available is the daily new cases of recorded infectious people. Since the available data does not contain the recorded cases at the border by Antigen test, we only fit the data with the locally generated cases. Using our model, the recorded local new infections generated at time t, D(t), can be computed using the following equation:

$$D(t) = \delta\theta E(t)$$

We solve the system of differential equations numerically using a fourth order Runge-Kutta method. We use the solutions to obtain the best-fit parameters via a nonlinear least squares regression method that minimizes the following sum of the squared residuals:

$$L(\phi, \beta_1, \beta_2, \theta, \tau) = \sum_{i=1}^{n} [D(t_i) - \overline{D}(t_i)]^2$$

where $D(t_i)$ and $\overline{D}(t_i)$ are the new cases of infectious people who have been recorded, predicted by the model, and those given in the available data, respectively, and $\phi, \beta_1, \beta_2, \theta, and\ \tau$ are parameters to be estimated. Here, n represents the total number of data points used for the model fitting. In our study, all computations were carried out in MATLAB 2021a (The MathWorks, Inc.).

Effective reproduction number from data

There are several ways to calculate the basic reproduction rate using data on disease incidence. The maximum likelihood method (MLM), developed by White and Pagano is one of them and is frequently used in studies (Cori *et al.*, 2013; You *et al.*, 2020). We also calculated the effective reproduction number R_t from the daily incidence data as a marker for the decrease or surge in infections from the real-time data. Time-varying R_t can be calculated using the time series of the infections and generation time distribution (Cori *et al.*, 2013). We used the approach developed by Thompson for the estimation of effective reproduction numbers using the EpiEstem package of the R program (Thompson *et al.*, 2019). Based on the previous study (Adhikari *et al.*, 2022), we used the mean serial interval to be 4.7 days with a standard deviation of 2.9 days.

RESULTS AND DISCUSSION

Analysis of the model

In this section, we discuss the analytic properties of the given system.

Positivity and boundedness of the system

Theorem 3.1: If *S(0) > 0, E(0) > 0, IR(0) > 0, IN(0) > 0, R(0) > 0, M(0) > 0* then the set of solution *S(t), E(t), IR(t), IN(t), R(t), M(t)* of the system (1-6) exist, remain non-negative and bounded, for all $t \ge 0$.

Proof: In order to show positivity, for $t > 0$, we have from equation (1)

$$\frac{dS}{dt} = \Lambda + \lambda(1-\tau)(1-\phi)\,M + \lambda(1-\rho)\,\phi\,M - \frac{(\beta_1 I_R + \beta_2 I_N)dt}{(S + E + I_R + I_N + R)} - \mu S$$

$$\frac{dS}{dt} \ge -\frac{(\beta_1 I_R + \beta_2 I_N)dt}{(S + E + I_R + I_N + R)} - \mu S$$

$$\Rightarrow \int_0^t \frac{dS}{S} \ge -\int_0^t \frac{(\beta_1 I_R + \beta_2 I_N)dt}{(S + E + I_R + I_N + R)}$$

$$\Rightarrow ln\frac{S(t)}{S(0)} \ge -\int_0^t \frac{(\beta_1 I_R + \beta_2 I_N)dt}{(S + E + I_R + I_N + R)}$$

$$\Rightarrow S(t) \ge S(0)e^{-\int_0^t \frac{(\beta_1 I_R + \beta_2 I_N)dt}{(S + E + I_R + I_N + R)}}$$

$$\Rightarrow S(t) \geq S(0)e^{-\int_0^t \frac{(\beta_1 I_R + \beta_2 I_N)dt}{(S+E+I_R+I_N+R)}}$$

Thus, S*(t) > 0*; as, $t \to \infty$.
From equation (2)

$$\frac{dE}{dt} = \frac{(\beta_1 I_R + \beta_2 I_N) S}{S + E + I_R + I_N + R} - \delta E - \mu E$$

$$\Rightarrow \int_0^t \frac{dE}{E} \geq -\int_0^t (\delta + \mu) dt$$

$$\Rightarrow E(t) \geq E(0)e^{-\delta+\mu)t}$$

$$\Rightarrow E(t) \geq 0 \,, \forall\, t > 0$$

As $t \to \infty$, we get, $E(t) \geq 0$.

Similarly, we can show that $I_R(t) \geq 0$, $I_N(t) \geq 0$, $R(t) \geq 0$, $M(t) \geq 0$
To show boundedness:
Let us suppose that total population is N = S + E + I_R + I_N + R + M.
Adding all differential equations (1-6), we get

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dM}{dt} + \frac{dE}{dt} + \frac{dI_R}{dt} + \frac{dI_N}{dt} + \frac{dR}{dt}$$

$$\frac{dN}{dt} \leq \boldsymbol{\lambda} - \mu \boldsymbol{N}$$

$$\frac{dN}{dt} + \mu \boldsymbol{N} \leq \boldsymbol{\lambda}$$

$$\int_0^t d(Ne^{\mu t}) \leq \int_0^t e^{\mu t} \lambda dt$$

$$N(t) = N(0)e^{-\mu t} + \frac{\lambda}{\mu} - \frac{\lambda}{\mu} e^{-\mu t}$$

As, $t \to \infty$, $e^{-\mu t} = 0$.
Hence, $N(t) \leq \frac{\lambda}{\mu}$. Thus, *N(t)* is bounded.
Similarly, we can show that *S, E, I_R, I_N,* R, and *M* are bounded.

Disease free equilibrium

At disease free equilibrium, there is no disease at any compartment. So, I_R = I_N = E =0, and ϱ = τ = ф=0;
Solving for S, R, M,

$$\frac{dS}{dt} = 0; \frac{dM}{dt} = 0; \frac{dR}{dt} = 0;$$

we get, $S^0 = \frac{\lambda}{\mu}$, $R^0 = 0$, $M^0 = 0$. Hence, we get $\varepsilon^0 = \left(\frac{\lambda}{\mu}, 0, 0, 0, 0, 0\right)$ as diseases free equilibrium point.

Reproduction Number

First, we calculated the diseases free equilibrium point. At the disease-free equilibrium point the portion of positive antigen test is zero, i.e. ϱ = 0, τ = 0, and we use the pre-pandemic condition λ = λ (0), and $E = I_R = I_N = 0$. We get the following disease-free equilibrium point: $\varepsilon^0 = (S^0, 0, 0, 0, 0, 0)$, where S^* = N be the total population of the Sudurpashchim province.

We divide the compartments into two groups: infected $\vec{X} = (X_i, i = 1, 2, 3)$ (Exposed, Recorded Infectious and Non-recorded Infectious) and non-infected $\vec{Y} = (Y_j, j = 1, 2, 3)$ (Susceptible, Recovered and Migrant workers). Then the system (1-6) can be written as: $X'_i = f_i(\vec{X}, \vec{Y})$, and $Y'_i = g_j(\vec{X}, \vec{Y})$, for $i = 1,2,3,\ j = 1,2,3$. The right-hand side of the system of infected compartments can be written as:

$fi(\vec{X}, \vec{Y}) = F_i(\vec{X}, \vec{Y}) - V_i(\vec{X}, \vec{Y})$, where $F_i(\vec{X}, \vec{Y})$ contains the terms representing the new infections in compartment i and $V_i(\vec{X}, \vec{Y})$ contains the terms containing the difference between the transfer of individuals out of and into the compartment i. Then we construct the following two matrices using

$F = \frac{\partial F_i}{\partial X_i}$ and $V = \frac{\partial V_i}{\partial X_i}$ at the diseases free equilibrium (DFE) point as follows:

$$F = \begin{bmatrix} 0 & \beta_1 & \beta_2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, V = \begin{bmatrix} \delta + \mu & 0 & 0 \\ -\delta\theta & \eta + \mu + \chi_1 & 0 \\ -\delta(1-\theta) & 0 & \eta + \mu + \chi_2 \end{bmatrix}.$$ Then we have

$$V^{-1} = \begin{bmatrix} \frac{1}{\delta+\mu} & 0 & 0 \\ \frac{\delta+\theta}{(\delta+\mu)(\eta+\mu+\chi_1)} & \frac{1}{(\eta+\mu+\chi_2)} & 0 \\ \frac{\delta(1-\theta)}{(\delta+\mu)(\eta+\mu+\chi_2)} & 0 & \frac{1}{\eta+\mu+\chi_2} \end{bmatrix}, \text{ and}$$

$$FV^{-1} = \begin{bmatrix} \frac{\beta_1\delta\theta}{(\delta+\mu)(\eta+\mu+\chi_1)} + \frac{\beta_2\delta(1-\theta)}{(\delta+\mu)(\eta+\mu+\chi_2)} & \frac{\beta_1}{(\eta+\mu+\chi_2)} & \frac{\beta_2}{\eta+\mu+\chi_2} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

The largest eigenvalue of the matrix FV^{-1} gives the basic reproduction number as follows:

$$R_0 = \frac{\beta_1\delta\theta}{(\delta+\mu)(\eta+\mu+\chi_1)} + \frac{\beta_2\delta(1-\theta)}{(\delta+\mu)(\eta+\mu+\chi_2)} = R_1 + R_2;$$

Where $R_1 = \frac{\beta_1\delta\theta}{(\delta+\mu)(\eta+\mu+\chi_1)}$, and $R_2 = \frac{\beta_2\delta(1-\theta)}{(\delta+\mu)(\eta+\mu+\chi_2)}$.

We can interpret the two terms as representing the two routes of transmission through the reported infections (first term) and non- reported infections (second term). The corresponding effective reproduction number is

$$R_t = \left(\frac{\beta_1\delta\theta}{(\delta+\mu)(\eta+\mu+\chi_1)} + \frac{\beta_2\delta(1-\theta)}{(\delta+\mu)(\eta+\mu+\chi_2)}\right)\frac{S(t)}{N(t)}$$

Stability of disease-free equilibrium point

As expected, we are able to theoretically establish R_0 as the outbreak threshold for our model, as stated in the following theorem:

Theorem 3.2. Disease free equilibrium point of the system of equations (1-6) is asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof. Jacobian of the system of equations (1-6) evaluated at the disease-free equilibrium, ε^0, is

$$\begin{bmatrix} -\mu & 0 & -\beta_1 & -\beta_2 & 0 & \lambda(1-\theta)+\lambda\theta \\ 0 & -\delta-\mu & \beta_1 & \beta_2 & 0 & 0 \\ 0 & \delta\theta & -\eta-\mu-\chi_1 & 0 & 0 & 0 \\ 0 & \delta(1-\theta) & 0 & -\eta-\mu-\chi_2 & 0 & 0 \\ 0 & 0 & \eta & \eta & -\mu & 0 \\ 0 & 0 & 0 & 0 & 0 & -\lambda \end{bmatrix}$$

Clearly, - μ , - μ , and -**λ** are three eigen-values of this Jaccobian. For the remaining three eigen values we solve the following characteristic equation:

$a_0P^3 + a_1P^2 + a_2P + a_3 = 0,$
Where, $a_0 = 1, a_1 = \delta + 2\eta + 3\mu + \chi_1 + \chi_2,$
$a_2 = \eta^2 + 2\eta\mu + \eta\chi_1 + \eta\chi_2 + \mu^2 + \mu\chi_1 + \mu\chi_2 + (1 - R_1)(\delta\eta + \delta\mu + \delta\chi_1 + \eta\mu + \mu^2 + \mu\chi_1) + (1 - R_2)(\delta\eta + \delta\mu + \delta\chi_2 + \eta\mu + \mu^2 + \mu\chi_2 + \chi_1\chi_2)$
And, $a_3 = (1 - R_0)(\delta + \mu)(\eta + \mu + \chi_1)(\mu + \mu + \chi_2)$
Also, $a_1a_2 - a_3a_0 = A(1 - R_1) + B(1 - R_2) + CR_0$
Where, $A = \chi_1(3\delta^2 + 5\delta\eta + \chi_2(\delta + \mu) + \delta\mu + 3\eta\mu + 4\mu^2) + \delta^2\eta + \delta^2\mu + 2\delta\eta^2 + \chi_2(\delta + \mu)(\eta + \mu) + \delta\eta\mu + 4\delta\mu^2 + \chi_1^2(\delta + \mu) + 2\eta^2\mu + 5\eta\mu^2 + 3\mu^3$,
$B = (\delta + \mu)(\eta + \mu + \chi_2)(\delta + 2\eta + 3\mu + \chi_1 + \chi_2),$
$C = (\delta + \mu)(\eta + \mu + \chi_1) + (\eta + \mu + \chi_2).$
So, as $R_1 < 1$, and $R_2 < 1$; $a_1 > 0, a_2 > 0$, $a_1a_2 - a_3a_0 > 0$ *and for* $R_0 < 1, a_3 > 0.$
Hence by Routh-Horwitz criteria, the DFE is locally asymptotically stable.

Existence of endemic equilibrium point(s) of the model

Let $E^*= (S^*, E^*, I_R^*, I_N^*, R^*, M^*)$ be the corresoponding arbitrary endemic equilibrium point of the model (1-6) and let $\Psi = \frac{\beta_2 I_N^* + \beta_1 I_R^*}{S^* + I_N^* + I_R^* + E^* + R^*}$

And solving the system (1-6) making its right-hand side equal to zero, we get:

$$S^* = \frac{\Lambda}{\mu + \Psi}$$

$$E^* = \frac{\Lambda\Psi}{(\mu + \delta)(\mu + \Psi)}$$

$$I_R^* = \frac{\delta\theta\Psi\Lambda}{(\delta + \mu)(\mu + \Psi)(\eta + \mu + \chi_1)}$$

$$I_N^* = \frac{\delta\,(1 - \theta)\,\Psi\Lambda}{(\delta + \mu)(\mu + \Psi)(\eta + \mu + \chi_2)}$$

$$R^* = \frac{\delta\eta\Psi\Lambda}{\mu\,(\delta + \mu)(\mu + \Psi)(\eta + \mu + \chi_2)}$$

$$M^* = 0$$

Now substituting these values of $(S^*, E^*, I_R,\ I_N^*, E^*, R^*)$ in the expression of Ψ gives Ψ = 0 which leads the disease-free equilibrium point and the following quadratic equation:

$a\Psi^2 + b\Psi + c = 0$, where,

a = χ_1 ((η + μ) (δ (1 - θ) +μ) + μ Ψ^2) +(η + μ) ((δ + μ) (η + μ) + χ_2 (δ θ + μ))>0

b = μ (χ_1 ((η + μ) (δ (2 – θ) + 2μ) + χ_2 (δ +2μ) + (η + μ) (2(δ + μ) (η + μ) + χ_2 (δ θ + δ + 2μ)))>0

c = $\Lambda\,\mu^2\,(1 - R_0)\,(\delta + \mu)\,(\eta + \mu + \chi_2)\,(\eta + \mu + \chi_1) < 0, if\ R_0 > 1.$

This shows that Ψ gives the positive roots if R₀ >1. Thus, we have the endemic equilibrium point $E^* = (S^*, E^*, I_R^*, I_N^*, R^*, M^*)$, if R₀ >1.

Numerical simulation of the model

In this section, we fit the model with real time data of COVID-19 of Sudurpashchim province and estimate the values of some parameters. We also examine the effects of control measures on the reduction of epidemic burden.

Epidemic pattern and model validation

We fitted our model to daily recorded new cases data of Sudurpashchim, Nepal from April 1 to August 31, 2021), and estimated five parameters $\phi, \beta_1, \beta_2, \theta, and\ \tau$. The values of the best estimates along with all other parameters and state variables are provided in Table 1. As shown in Fig.5 (left) the model has an excellent agreement with the data of recorded new cases. In addition, we estimated the cumulative cases of COVID-19 during the period of study and compared our estimates with the data (Fig. 5, right).

Our model is capable of accurately predicting the cumulative cases of COVID-19 in Sudurpashchim province, thereby validating our modeling approach. We estimated extremely low (2%) detection of new cases. We estimated only 10% border screening with Antigen tests among the returnees of Sudurpashchim from India during the Delta surge which was not sufficient to lower the burden of the pandemic. Antigen detection among returnees at the border reveals ~10% positivity rate, which is incredibly high and is most likely caused by the identification of suspected cases who had some symptoms. We calculated that the detection rate inside the Sudurpashchim province was exactly the same as the rate among unscreened migrants, which we estimated to be only ~ 2%.

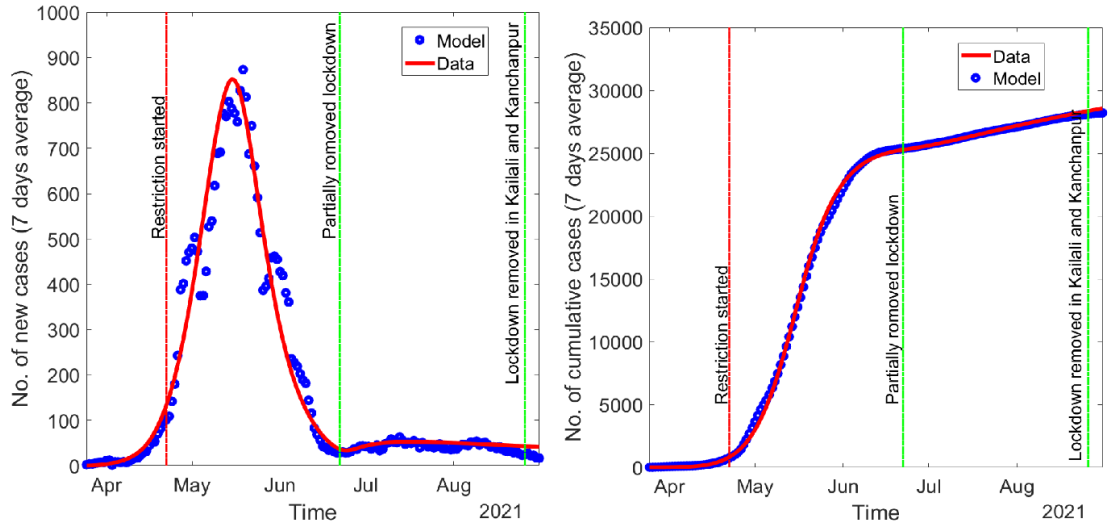

Figure 5. Model fitting with recorded new cases of COVID-19 (left) and the consistency of cumulative data of recorded cases with the model (right)

Table 1. Values of state variables estimated and fixed parameters

Description of state variables/Parameters	Symbols	Base Values	References
Susceptible population	S(0)	1377811	Calculated
Recovered population	R(0)	833357	Calculated
Migrant population	M(0)	500000	Calculated
Exposed population	E(0)	20	Assumed
Recorded infectious population	$I_R(0)$	12	Assumed
Non-Recorded infectious population	I_N (0)	80	Assumed
Positive rate in Antigen test	ρ	0.1	Calculated
Migration rate to Nepal	λ	0.002	Calculated
Recorded death	χ_1	0.0012	Calculated
Non-Recorded death rate	χ_2	0.0001	Estimated
Transmission rate of recorded infectious	β_1	0.125	Estimated
Transmission rate of non-recorded infectious	β_2	0.615	Estimated
Detection rate of local cases	θ	0.02	Estimated
Positivity of non-recorded cases from India	τ	0.02	Estimated
Antigen test rate	ϕ	0.1	Estimated
Latency period	$\frac{1}{\delta}$	5 days	(Hossain *et al.*, 2020)
Infectious period	$\frac{1}{\eta}$	12 days	(Linton *et al.*, 2020)
Reduction rate of transmission of non-recorded infectious	r, r_1	0.067, 0.05	Estimated

Effective reproduction number

Using the Maximum Likelihood Method (MLM), we first estimated the reproduction number R_t from the data. Before the lockdown, R_t was seen to reach up to 2.63 (95% CI [2.38-2.89]) on April 19, 2021. This finding suggests that there had already been significant community transmission of the disease prior to the lockdown. R_t estimated from the data offers insightful information about the disease trend, but it excludes infections brought on by non-detected cases, which may be the primary disease super-spreader. To get around this restriction, we also used our model to estimate the time-dependent reproduction number (R_t). Because of the infections from non-recorded cases, the model accurately predicted a higher value of the reproduction number of 4.8 at the beginning of the Delta surge. R_t then rapidly declines after the lockdown is initiated. It dropped below threshold value 1 around the Mid of May 2021. Excellent agreements exist between this model's (R_t) trend and the trends of new cases.

Effect of border screening and lock-down

The Government of Nepal started the lock-down in Kathmandu Valley, the nation's capital, on April 29, 2021, after starting to raise new cases. The lock-down was immediately implemented in the Kailali and Kanchanpur districts of the Sudurpashchim province and soon expanded to the other districts. So, Border screening and lock-down were the two non-pharmaceutical control measures. The figures demonstrate the effectiveness of interventions in reducing the pandemic in the Sudurpashchim province.

Figure (7) (a) demonstrates how the effective reproduction rate dropped quickly as a result of the control interventions and reached below the cutoff value one, 3-4 days earlier than in the absence of policies. Figure (b), (c) and (d), show how well the control strategies reduced the number of cases. It demonstrates that border screening was ineffective at reducing cases in the absence of a lockdown. The number of new, active, and cumulative cases would have remained unchanged in the absence of the lockdown and the two control interventions. Without lockdown, the number of daily new cases at the peak time would be increased from 864 to 1303, the number of active cases from 7805 to 10987, and the total number of cases until August 31, 2021, from 28564 to 32571. Thus, control interventions reduced 34% of new cases, 28% of active cases during the peak time and overall cases by 12.3% until August 2021.

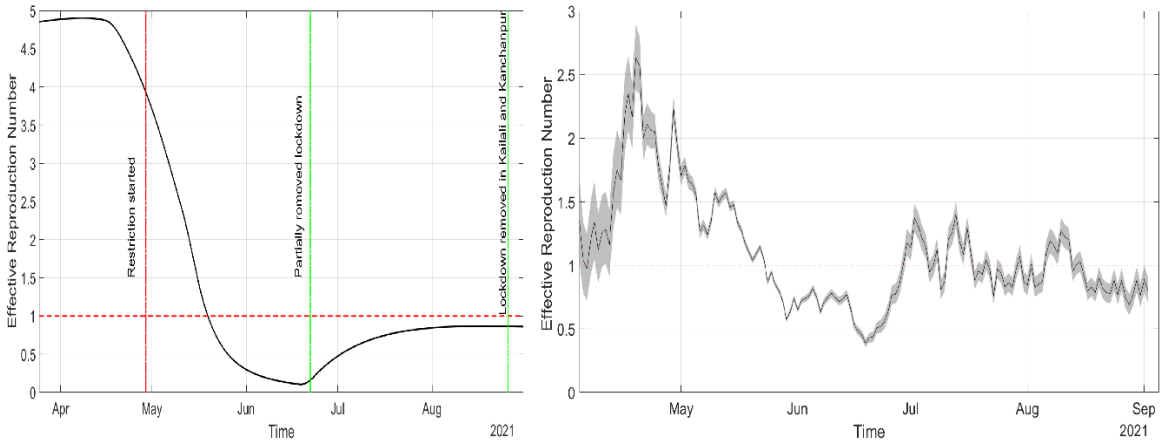

Figure 6. Effective reproduction number from model (left) and from the data (right)

Since, we have data on the number of cases in hospitals across the Sudurpashchim province. To estimate the potential hospital burden that would exist in the absence of control interventions, we used this data. The actual and potential hospitalization in the absence of control interventions is represented in Fig. 8 given below.

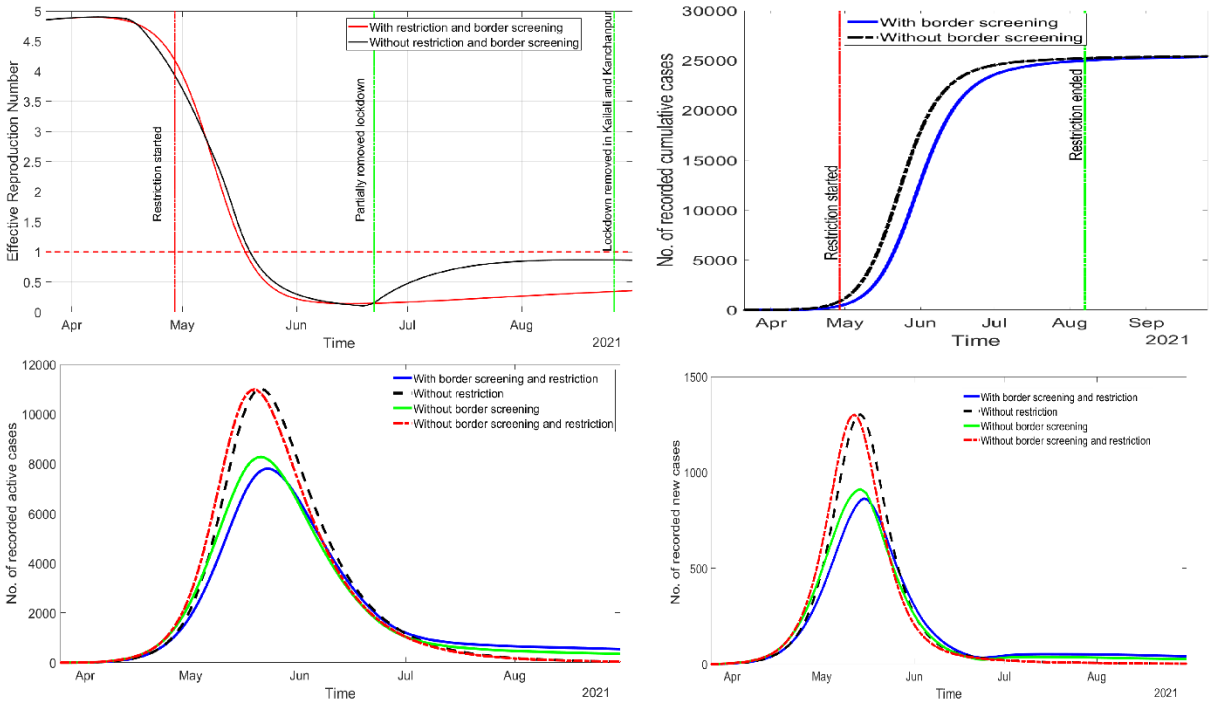

Figure 7. Effect of the control measures on the reduction of (a) reproduction number (b) daily new cases (c) active cases and (d) total number of cases are given in Figure below

The potential hospitalization cases are calculated as:

$$\text{The potential hospitalization cases at time (t)} = \frac{H \times T_W}{T_C}$$

Where, H: Hospitalization at time (t),

T_C: Total recorded active cases with control measures at time (t)

T_W: Total recorded active cases without control measures at time (t).

Similarly, we estimated ICU and Ventilator cases. The results show that the intervention policies have significantly reduced the number of hospital cases. If no actions were taken, at the peak of the pandemic, there would be an increase in the number of patients in normal beds from 1594 to 2024, in ICUs from 51 to 67, and on ventilators from 15 to 20. As a result, during the peak of the pandemic, control interventions reduced the number of patients in regular beds by ~ 27%, ICU admissions by ~31%, and ventilator cases by ~33%.

Non-pharmaceutical interventions are the only way to control new and frequent outbreaks of pandemics with new strains in the absence of an effective vaccine or drug therapy. Each of the more than 200 countries that were impacted by COVID-19 first and second waves uniquely responded to the crisis in a unique way making it challenging to assess the efficacy of the measures. We developed the deterministic mathematical model validated with the data of Sudurpashchim, Nepal and estimated key parameters of the disease dynamics. We then used the model for a retrospective analysis of measures taken to combat the spread of the disease, to evaluate their impact.

We only estimated 10% of returnee migrants had antigen tests at the border, so this number of border screenings was insufficient to reduce epidemics. Some studies (Zhang *et al.*, 2021; Aronna *et al.*, 2022) also show that the direction of COVID-19 cases is significantly low in other places as well. We also estimated that the number of recorded cases is significantly low (2%), which also lowers the effectiveness of border screening, therefore, border screening is useless without meticulous contract tracing and the detection asymptomatic cases as well. However, the lockdown was successful in reducing the pandemic's peak, overall size, and hospital cases. Our findings are consistent with many other studies (Aljazeera, 2021; Shrestha & Mandal, 2020; Shiraef *et al.*, 2022). However, due to border screening along with lockdown, and contract tracing, the number of COVID-19 cases in Nepal during the first wave of the disease was significantly decreased (Adhikari *et al.*, 2021b; Pantha *et al.*, 2021).

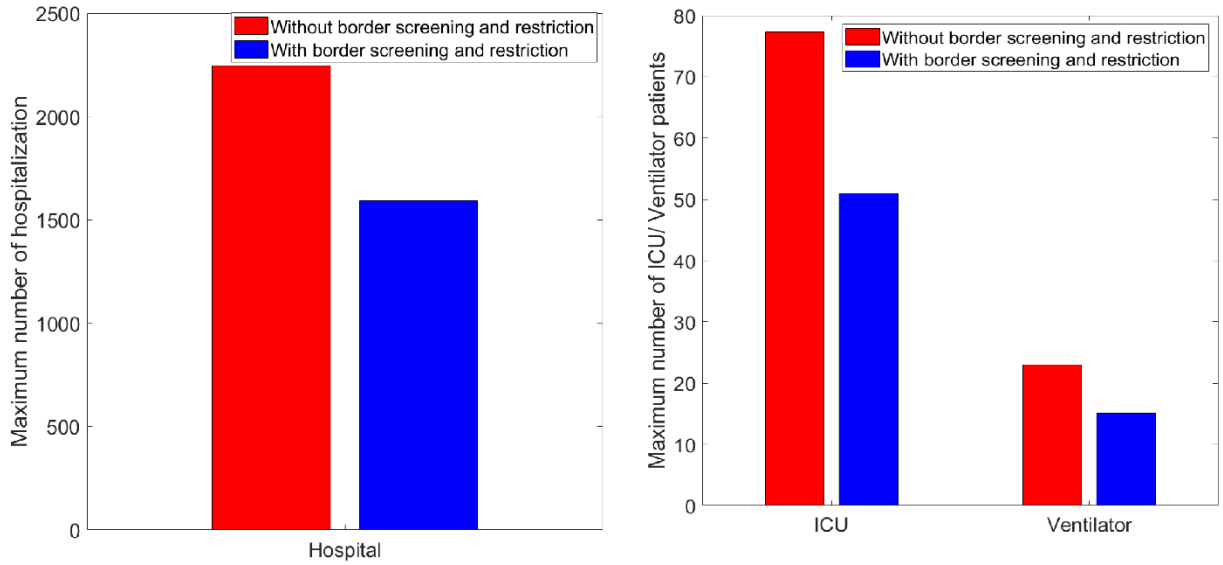

Figure 8. Effect of control measures on the reduction of hospitalization cases (left) ICU and ventilator cases (right) during the peak of the epidemic

We acknowledge some limitations of our study. We made use of the limited publicly accessible data sets from the Nepalese Ministry of Health and Population. The information on border screening must be carefully considered due to inadequate border policy. The findings of our model will be enhanced by the exact border screening and quarantine data. However, we examine the parameter's sensitivity over a wider range.

CONCLUSIONS

In conclusion, although cross-border mobility prohibitions and screening have a significant impact on infection transmission and spread, they have only a small effect on reducing the overall number of infections in the country because a significant number of infectious people are exposed to a stronger force of infection. When border screening and internal movement limitations are integrated, new case detection is quite successful. It is advisable to promote additional NPIs such as self-quarantine, telework, at-home case isolation, and social event limits during the contagious pandemic.

ACKNOWLEDGEMENTS

The work of KA, AP and RG is supported by the GRAID (Graduate Research Assistantship in Developing

countries) award from the International Mathematical Union (IMU). KA acknowledges the Nepal Academy of Science and Technology (NAST) for Ph. D. Fellowship. RG acknowledges the University Grants Commission (UGC) Nepal for Ph. D. Fellowship 2021.

AUTHOR CONTRIBUTIONS

NBC: conceptualization, formal analysis, investigation, methodology, numerical simulation, writing - original draft; KH: conceptualization, formal analysis, review, and editing; RG: conceptualization, review, and editing; AP: conceptualization, review, and editing; KNU: conceptualization, formal analysis, supervision, review, and editing.

CONFLICT OF INTEREST

There is no conflict of interest between the authors in this publication.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

REFERENCES

Adhikari, K., Gautam, R., Pokharel, A., Dhimal, M.N., Uprety, K.N., & Vaidya, N.K. (2022). Insight into Delta variant dominated second wave of COVID-19 in Nepal. *Epidemics*, *41*, 100642. https://doi.org/10.1016/j.epidem.2022.100642.

Adhikari, K., Gautam, R., Pokharel, A., Uprety, K.N., & Vaidya, N.K. (2021). Transmission dynamics of COVID-19 in Nepal: Mathematical model uncovering effective controls. *Journal of Theoretical Biology*, *521*(07), 110680.

Adhikari, K., Gautam, R., Shrestha, D.B., & Pokharel, A. (2021). Transmission Dynamics of COVID-19 in Nepal. *Humanities and Social Sciences Journal*, *521*(07), 155-169.

Aljazeera. (2021). Nepal starts 15-day covid lockdown as infectious spike. Retrieved 07 October 2021 from Aljazeera: https://www.aljazeera.com/news.

Aronna, M., Soledad, R.G., & Moschen, L.M. (2022). Aronna, Maria Soledad, Roberto Gugli Estimate of the rate of unreported COVID-19 cases during the first outbreak in Rio de Janeiro. *Infectious Disease Modelling*, *7*(3), 317-332.

CBS. (2022). Nepal Statistical Yearbook 2021. Central Bureau of Statistics, Government of Nepal. Retrieved 3 January 2022, from https://cbs.gov.np/wp-content/upLoads/2022/09/Statistical-Year-Book-Final.pdf.

Cori, A., Neil, F.M., Chrisophe, F., & Simon, C. (2013). A new framework and software to estimate time-varying reproduction numbers during epidemics. *American Journal of Epidemiology*, *178*(9), 1505–1512. https://doi.org/10.1093/aje/kwt133.

Ewen, C. (2021). Delta coronavirus variant: scientists brace for impact. *Nature*, *595*(7865), 17-18.

Gautam, R., Pokharel, A., Adhikari, K., Uprety, K.N., & Vaidya, N.K. (2022). Modeling malaria transmission in Nepal: impact of imported cases through cross-border mobility. *Journal of Biological Dynamics*, *16*(1), 528-564.

Hossain, M.P., Junus, A., Zhu, X., Jia, P., Wen, T.-H., Pfeiffer, D., & Yuan, H.-Y. (2020). The effects of border control and quarantine measures on the spread of covid-19. *Epidemics*, *32*, 100397.

Kang, M., Xin, H., Yuan, J., Ali, S.T., Liang, Z., Zhang, J., Hu, T., Lau, E.H., Zhang, Y., Zhang, M., Cowling, B.J., & Wu, P. (2021). Transmission dynamics and epidemiological characteristics of SARS-CoV-2 Delta variant infections in Guangdong, China. *Eurosurveillance*, 27(10), 2100815.

Khare, V. (2021). India's Kumbh festival attracts big crowds amid devastating second Covid wave. Retrieved 3 January 2022 from https://www.bbc.com/news/world-asia-india-56770460.

Kunwar, L.S. (2015). Emigration of Nepalese people and its impact. *Economic Journal of Development Issues*, *19*(1-2), 77-82.

Linton, N.M., Kobayashi, T., Yang, Y., Hayashi, K., Akhmetzhanov, A.R., Jung, S.-M., Yuan, B., Kinoshita, R., & Nishiura, H. (2020). Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right. *Journal of Clinical Medicine*, *9*(2), 538.

Mindermann, S., Sharma, M., Whittaker, C., Mellan, T.A., Thomas, W., & Mishra, S. (2021). Changing composition of SARS-CoV-2 lineages and rise of Delta variant in England. *EClinicalMedicine*, *39*, 101064. https://doi.org/10.1016/j.eclinm.2021.101064.

MoHP. (2021a). Health Sector Response to COVID-19. Retrieved 04 January 2022 from https://covid19.mohp.gov.np/.

MoHP. (2021b). Nepal National Sero-Prevalence Survey for COVID-19 October 2020. Kathmandu: Government of Nepal, Ministry of Health and Population.

Nebehay, S., & Farge, E. (2021). WHO classifies India variant as being of global concern. Retrieved 15 May 2021 from https://www.reuters.com/business/healthcare-pharmaceuticals/who-designates-india-variant-being-global-concern-2021-05-10/.

Neupane, P., Bhandari, D., Tsubokura, M., Shimazu, Y., Zhao, T., & Kono, K. (2021). The Nepalese health care system and challenges during COVID-19. *Journal of Global Health*, *11*, 03030. https://doi.org/10.7189/jogh.11.03030.

Pantha, B., Acharya, S., Joshi, H.R., & Vaidya, N.K. (2021). Inter-provincial disparity of COVID-19 transmission and control in Nepal. *Scientific Reports*, *11*(1), 13363.

Pokharel, A., Adhikari, K., Gautam, R., Uprety, K.N., & Vaidya, N.K. (2022). Modeling transmission dynamics of measles in Nepal and its control with monitored

vaccination program. *Mathematical Biosciences and Engineering*, *19*(8), 8554-8579.

Poudel, K.C., Okumura, J., Jimba, M., Sharma, M., & Wakai, S. (2004). Migration in far western Nepal: a time bomb for a future HIV/AIDS epidemic. *Tropical Doctor*, 34(1), 30-31.

Prasain, S. (2021). Nepal's lockdown 2.0, new Covid curbs on travel. Retrieved 4 May 2022 from https://kathmandupost.com/money/2021/04/28/explained-nepal-s-lockdown-2-0-new-covid-curbs-on-travel.

Sara, H., Din, M., Zia, F., & Khan, Z.S. (2021). Emerging concerns regarding COVID-19; second wave and new variant. *Journal of Medical Virology*, *93*(07), 4108-4110.

Shiraef, M.A., Friesen, P., Feddern, L., & Weiss, M.A. (2022). Did border closures slow sars-cov-2? *Scientific Reports*, *12*(1), 1709. https://doi.org/10.1038/s41598-022-05482-7.

Shrestha, P., & Mandal, C. (2020). With hundreds of thousands of migrants predicted to return home, nepal needs to brace for a crisis. the. Retrieved 5 April 2021 from https://kathmandupost.com/national/2020/04/22/with-hundreds-of-thousands-of-migrants-predicted-to-return-home-nepal-needs-to-brace-for-a-crisis.

Sudurpashchim Khabar. (2021a). Still, Sudurpashchim has a similar crowd. Retrieved 7 August 2021 from Sudurpashchim Khabar: https://sudurpashimkhabar.com/2021/05/16/38301/.

Sudurpashchim Khabar. (2021b). There is a severe oxygen shortage in the Attaria Kailali community hospital, making it difficult to save the patients. Retrieved 4 May 2022 from Sudurpaschim Khabar: https://sudurpashimkhabar.com/2021/05/12/37859/.

Thompson, R., Stockwin, J., van Gaalen, R., Polonsky, J., Kamvar, Z., Demarsh, P., Dahlqwist, E., Li, S., Miguel, E., Jombart, T., Lessler, J., Cauchemez, S., & Cori, A. (2019). Improved inference of time-varying reproduction numbers during infectious disease outbreaks. *Epidemics*, *29*, 100356.

Vaidya, N.K., & Wu, J. (2011). HIV epidemic in Far-Western Nepal: effect of seasonal labor migration to India. *BMC Public Health*, *11*, 1-11.

WHO. (2021). COVID-19 weekly epidemiological update, edition 45. Retrieved 7 April 2021 from https://apps.who.int/iris/bitstream/handle/10665/342009/CoV-weekly-sitrep22Jun21-ng.pdf?sequence=1

Worldometer. (2021). Coronavirus Cases. Retrieved 6 7, 2021, from Worldometer: https://www.worldometers.info/coronavirus/.

You, C., Deng, Y., Hu, W., Sun, J., Lin, Q., Zhou, F., Pang, C.H., Zhang, Y., Chen, Z., & Zhou, X.-H. (2020). Estimation of the time-varying reproduction number of covid-19 outbreak in China. *International Journal of Hygiene and Environmental Health*, *228*,113555. https://doi.org/10.1016/j.ijheh.2020.113555.

Zhang, X.-S., Vynnycky, E., Charlett, A., De Angelis, D., Chen, Z., & Liu, W. (2021). Transmission dynamics and control measures of covid-19 outbreak in China: a modelling study. *Scientific Reports*, 11, 2652. https://doi.org/10.1038/s41598-021-81985-z.